butions (e.g. hospital stays). Therefore, estimates of uncertainty must be factored into economic facets of HTAs.

CONFLICT OF INTEREST STATEMENT: Mr. Paul Trueman is a Director of York Health Economics Consortium, The University of York and it can be confirmed that there is no conflict of interest involved in this paper nor in his participation in this entire event.

References:

1. Deloitte Center for Health Solutions and Deloitte Consulting LLP. Targeted therapies: navigating the business challenges of personalized medicine, 2007. <www.deloitte.com/dtt/cda/doc/content/us_chs_targetedTherapies_012307%281%29.pdf>.
2. European Network for HTA (EUnetHTA). HTA definition. <http://www.eunethta.net/HTA/>.

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THE INDUSTRY–PAYER CHALLENGE OF NEXT-GENERATION ONCOLOGY DRUGS

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Industry, too, faces challenges as we enter the era of molecularly targeted therapy. Investment in the research and development can be significant, but a targeted therapy may be appropriate for only a subset of patients who have the correct molecular target. Screening would eliminate patients for whom the treatment would not be effective. As such, the development costs may increase but the potential patient population may decrease. Therefore, incentives need to be in place to ensure that manufacturers can realise a return on their investment.

Molecularly targeted therapy appears to offer an attractive value proposition; however, this can only be realised if industrial incentives are aligned with health care incentives. Introducing these therapies into practice presents some challenges. 'Both strong intellectual property protections and value-based, flexible pricing systems will be important in making personalised medicine a reality.'[2]

Health care expenditures, both in absolute terms and as a percentage of gross domestic product (GDP) are growing around the world. Innovative drugs are becoming more difficult to find, and more expensive to develop. Together these present significant challenges to both Payers and the Pharmaceutical Industry.

The challenge is developing successful next-generation oncology drugs within this environment. Success may be defined in several different ways. Success, to the patient, means access to a treatment that works. For the physician, it means using the right drugs in the right patients at the right time. Success, as defined by payers, connotes affordability and value for monies spent. Pharmaceutical companies seek success in the form of payback on their investment in research and development.

According to the traditional view of drug development and licensure, the product has three hurdles to negotiate: safety, efficacy and quality. In reality, however, at least three additional hurdles must be surmounted: national pricing and reimbursement, local/regional market access and health technology assessment (HTA). These last three include financial pressures in their evaluation. There is one additional challenge that must be considered at the outset of the development process – the need to measure value. To achieve success, pharmaceutical companies have to demonstrate that a product will deliver value (to the patient, and to the health economy) and net a return on their investment.

The highest hurdle is HTA, which has been defined as 'a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value.'[3] Nearly 50% of licensed therapies fail to fully surmount the HTA hurdle in some way.

Not all drugs need to be subjected to the same levels of rigorous evaluation. The amount and quality of evidence required for licensure varies, and evidence required to support drug pricing and market access follows a parallel track. For example, therapies that are initially innovative (with price based on the value delivered) are eventually joined in the market by other drugs that are therapeutically similar, resulting in cluster-based or reference pricing.

Payer–Industry partnerships could be an attractive, and potentially successful approach in the future, as well (Fig. 1). Much might be gained by leveraging complementary skills sets and through access to, and analysis of, comprehensive (real-world) treatment and outcomes data. Ultimately, payers and pharmaceutical firms are working for the same person – the patient.

SURMOUNTING THE HTA HURDLE: HTA poses a number of questions regarding new therapies. First, how is the new treatment or technology to be used? This line of questioning should include the potential role or position of the therapy, the patients most likely to benefit from it, when in the disease course should it be used, and for how long. In addition to clinical-efficacy and –effectiveness, questions of cost effectiveness and resource utilisation must be asked: How much does the therapy cost? Is it affordable? Does it represent acceptable 'value for money'? (i.e. is it cost effective?) What is the best way to allocate scarce resources? Evaluation of cost effectiveness is often one of the most important components of HTA.

Key concepts often addressed are affordability, value for money, and willingness to pay. Implicit are issues of rational

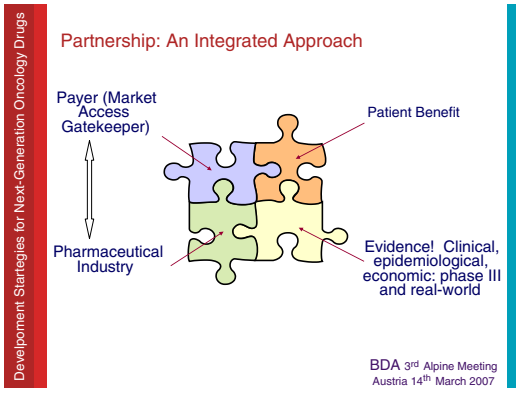

Fig. 1 – Payer–industry partnership: an integrated approach.

rationing and rational health care resource allocation. Industry does not like the notion of rationing, but it supports identifying the best use of medicines in terms of the most appropriate patients for the treatment and the most appropriate time in their disease progression or treatment. There is a significant role for BDA in working toward the aim of using biologics and biomarkers in identifying most appropriate target populations and the optimal time for treatment. Another key concept in HTA is reducing uncertainty, which decreases as the number of clinical studies evaluating safety and efficacy increases. HTA has a significant impact on data requirements. Meeting the HTA hurdle requires strong epidemiological evidence (i.e. the potential number of suitable patients), as well as an evidence-based position for the new agent in therapy or clinical guidelines. Ideally data are also necessary that identify the subpopulations that receive the greatest clinical benefit. Investigation of the agent must be based on meaningful endpoints and economic models must be transparent. Clinical trials must demonstrate its clinical efficacy and safety. Real-world studies must identify its clinical effectiveness. Finally, analysis of economic effectiveness of the agent must demonstrate its budget impact, cost effectiveness, cost utility and address equitable use. All supporting studies must include an indication of evidence quality.

A ROLE FOR BIOMARKERS AND SURROGATE ENDPOINTS IN HTA: How do clinical trial endpoints based on biomarkers figure into the development and licensure scheme? Biomarkers are surrogate endpoints that have substantial value in both clinical and HTA evaluations of new products. Biomarkers can be used to identify likely responding patients who have an abnormal condition prior to treatment initiation. They can also be used to assess the extent of disease, monitor the safety of an intervention, and evaluate the desired response.[1]

There are, however, some problems associated with reliance on surrogate rather than clinical endpoints in trials of anticancer agents. First, one must understand under what circumstances a surrogate endpoint provides both a qualitative and quantitative prediction of the clinical endpoint. Second, surrogate endpoints provide little or no information about the risk–benefit profile of the product and scant quantitative evidence of the magnitude of any effects on utility. For example, demonstrating an anti-tumour agent's significant effect on complete or partial response rates may have little relationship to its effect on either longevity or quality of life. The ultimate goal is to work toward patient benefit and measuring outcomes that are meaningful to, and valued by, the patient. Ideally the focus should evolve from patient reported outcomes to patient relevant outcomes.

CONFLICT OF INTEREST STATEMENT: Mr. Chris Teale is an employee of AstraZeneca Ltd. and it can be confirmed that there is no conflict of interest involved in this paper, nor in his participation in this entire event.

References:

1. Deloitte Center for Health Solutions and Deloitte Consulting LLP. Targeted therapies: navigating the business challenges of personalized medicine. 2007. <www.deloitte.com/dtt/cda/doc/content/us_chs_targetedTherapies_012307%281%29.pdf>.
2. Garrison Jr LP, Austin MJF. Linking pharmacogenetics-based diagnostics and drugs for personalized medicine. *Health Affairs* 2006;**25**:1281–90.
3. European Network for HTA (EUnetHTA). HTA definition. http://www.eunethta.net/HTA.

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THE BASIC ECONOMIC PROBLEM – INTERACTION OF ALL STAKEHOLDERS REQUIRED

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Demands are increasing on health care systems as the population ages and competition heats up among numerous branches. What data should serve as the basis for difficult decisions, and who should make them? Various financial barometers signal that burgeoning needs and shrinking resources will lead to scarcity (or perhaps, a perception of scarcity), and reimbursement is a central part of scarcity steering. To balance needs with available resources, we must establish priorities based on state, association and individual regulations.

Disease and scarcity are considered by people today to be unconquerable and omnipresent. The greater the knowledge people have of disease and its panoply of treatments, the greater is their awareness of the gap between demand and resources. Interestingly, the more society spends for disease management and meeting health-care needs, the larger the scarcity appears to be. Stated otherwise, being on the highest-ever level of material supply and per capita health-care spending for all ages in Europe, the topic of scarcity is being discussed more heatedly than at any other time.

For conventional cancer treatments for which response to treatment depends on the duration of treatment, the greatest value likely occurs near the beginning of treatment and decreases over time. The interest of payers is in reducing cost, and the interest of doctors and patients is in maximising treatment. Maximal medical care, of course, has higher costs. Optimal treatment, in an economic sense, occurs where the cost curve intersects the curve representing decreasing medical benefits over time. Payers, patients and doctors negotiate and compromise to arrive at the point of economically optimised medical care.

Predictive markers must be developed for molecularly targeted therapies to improve the benefit–cost relationship by only treating patients with a high expectation of response. For registration or licensure of new products, alternatives to randomised trials should be considered. Indirect comparisons might help facilitate patient access to new medicines. Also, it is important to keep in mind that molecularly targeted therapies mostly involve small populations. Randomised trials require a great deal of time, during which therapeutic options might change, thereby compromising the value of the trial's findings.

Academia, industry, regulators as well as patient advocacy groups and economists will have to act in concert, and scientific associations, such as the BDA will have to take active roles. Of para-